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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	**PAPER NUMBER**
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/637,149	MCDONNELL ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 22-29* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-13, 15-18, 22-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed 6/18/2007. The status of the claims is as follows: claims 1, 5-13, 15-18 and 22-29 are under current examination.

The following rejection is withdrawn:

35 USC 103 (Prusiner, Gassett et al, Nandi et al, Cai et al, Ernst and Race and US Patent Application 10/467591).

The Gassett et al reference has been withdrawn from this rejection because it appears that its teachings with respect to the conformational changes in PrP 27-30 induced by higher ionic strengths is are nebulous and thus, open to multiple interpretations. More specifically, this reference states the following: "Higher ionic strengths decreased absorption efficiency, almost certainly due to poor interaction of the protein sample with the ATR element. The conformational stability of PrP 27-30 with varying salt concentrations argues for the involvement of multiple molecular forces in the maintenance of amyloid polymer, a conclusion supported by studies of other amyloids" (pages 3-4). For example, it is not clear based on this recitation whether the poor interaction of the protein to element from a conformational change by a higher concentration of salt than by 0.25 M NaCl. And from the second statement, there is no indication that the conformational stability of the protein is either increased or decreased with either increases or decreases with salt concentrations. Further, to the ordinary artisan and by the teachings of the prior art, it is well known that salt alters the

secondary structure of proteins (by way of altering molecular forces) and this is further discussed in the rejection below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-13, 15-18 and 22-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prusiner (1982), Castle et al (1987), Nandi et al (2002), Cai et al (2002), Ernst and Race (1993) and US Patent Application 10/467591 (hereinafter as "Kritzler et al", 2002). The limitations of the rejected claims above are as follows:

1. a method of treating a body which is contaminated with prions by contacting the body with a composition comprising a phenol and a soluble inorganic salt to inactivate the prions;

2. wherein the phenol is up to 0.2M;

3. wherein the phenol has a log Pc value of 2 to 6.5, 2-5 and at least 4; 4. wherein the concentration of phenol is at least 10%; 5. wherein the soluble inorganic salt includes NaCl;

6. wherein the phenol includes o-phenylphenol and o-benzyl-p-chlorophenol; 7. wherein the phenol complexes with the prions and precipitates; 8. wherein the phenol has minimal solubility; 9. wherein the body includes a surface;

10. wherein the soluble inorganic salt is at a concentration of up to 5%;

11. wherein the composition further comprises a surfactant, more specifically, dodecylbenzene sulphonic acid;

12. wherein the composition further comprises an acidic sequestering agent; and

13. a method of treating a body contaminated with prions comprising contacting the body with a composition to inactivate prions, the composition comprising a phenol, co-solvent, water and a surfactant from the group of suphonic acids, sulfonates and combinations thereof.

Prusiner reviews six distinct treatments of a scrapie agent that leads to its inactivation, including treatment by phenol and chaotropic salts (see page 138). This reference discloses that "extraction with phenol, a potent denaturant of protein, under various salt and pH conditions destroyed infectivity" of the scrapie agent (see page

139). Prusiner concludes "denaturation of a protein within the scrapie agent leads to inactivation of the infectious particle". Thus, both phenol and salt, more specifically, guanidinium thiocyanate, have been shown to denature (alter the structure of) the scrapie agent that affects its function (infectivity). This reference does not disclose the detailed use of NaCl or of o- phenylphenol or o-benzyl-p-chlorophenol in order to inactivate prion proteins. This is found in the prior art as discussed below.

Castel et al teach the differential effects of purification methods with distinct condition on the aggregation of scrapie infectivity (see whole document). This study reveals that a purification procedure of pelleting such proteins in high concentrations of NaCl (e.g. 150 mM) leads to large aggregates with are only partially dispersed by sonication (see page 229). Additionally, Cai et al teach the solvent-dependent precipitation of prion protein in various pH, salt and ethanol concentration (see Abstract). High salt solutions (0.25 M) facilitated precipitation of both scrapie and cellular prion proteins (see page 31). Please note that precipitation and aggregation is due to the induction of conformational changes in the protein. Accordingly, Cai et al makes the following recitation: "In addition to pH, salt content plays a critical role in determining protein interactions in solution" (see page 34). Cai et al further suggests that the salt dependent precipitation may be due to "a dehydrated structure where hydrophobic interaction could be enhanced by NaCl" (see page 34). For further elucidation of this discussion, the Nandi et al reference is addressed here. This reference discusses the unfolding of the prion protein in various salt solutions at neutral pH (see entire document). Salt solutions, as disclosed by this reference, have large

effects on the structure and properties of proteins, including their solubility, denaturation and activity (see page 11020-1). This reference also provides the following recitation: "A considerable amount of studies on the effects of salts on the structural properties of proteins have been carried out in the past which suggest that at least two effects of salt, viz., their effect on solvent (water) structure and electrostatic interaction with charge groups of the protein, make major contributions to the structure-stabilizing properties of the proteins" (see page 11021). It would have been obvious to one of ordinary skill in the art to combine the teachings above in order to perform a method of inactivating prions using both phenol and salt at high concentrations. One would have been motivated to do so because both phenol and salt lead to the disruption of prion structure. The above references do not teach the specific use of o-phenylphenol and o-benzyl-p-chlorophenol in inactivating prions.

Ernst and Race teach a method in which the scrapie agent of brain homogenates is inactivated following treatment with LpH, or an aqueous phenolic disinfectant comprising both o-phenylphenol and o-benzyl-p-chlorophenol (see page 196). While this reference teaches using a concentration of 90% of LpH (page 197) which equates to 9% of phenolic derivative concentration (see 198 for conversion), varying the phenolic concentration would have been obvious to one of ordinary skill in the art in order to achieve optimal results of prion inactivation. Of note, the partition coefficient is dependent on the concentration value. The references above, however, do not teach a method using a composition that further comprises dodecylbenzene sulphonic acid.

Kritzler et al teach a method and a composition for treating a surface contaminated with a scrapie prion protein. The composition comprises one or more agents which favor the conformational unfolding of a scrapie prion protein (see Abstract), including inorganic salts and surfactants (see paragraphs 41 and 42). Dodecyl benzene sulfonate is disclosed in paragraph 41 as a denaturant that tends to "bind to proteins and initiate unfolding of tertirary structure". According to the instant specification, dodecylbenzene suphonic acid can be used as either a surfactant or as an acidic sequester agent. Further, Kritzler et al describe the use of a cosolvent, including m-Cresol (paragraph 39). A cosolvent is defined by the instant specification in paragraph 45 and includes a polyol which comprises only carbon, hydrogen and oxygen atoms. M-Cresol fit this definition. Kritzler et al disclose that such solvents "tend to denature, dissolve or swell proteins. Generally the products are not completely unfolded and possess an ordered conformation which differs from the native state" (paragraph 39).

Thus, it would have been obvious to one of ordinary skill in the art to combine the teachings of the references above in order to achieve a composition or a method of using such a composition comprising multiple agents that would alter the structure of the prion protein. One would have been motivated to combine various agents in order to denature the prion protein because as suggested by Kritzler et al "Many proteins are prone to loose their natural three dimensional folding pattern ("secondary and tertiary structure") and to become "denatured" The denaturation includes breakdown of the intramolecular interaction, especially hydrogen and disulphide bonds, and thus the loss

of the secondary structure which virtually all native proteins have in at least parts of the molecule, and which generally is decisively responsible for the activity of the protein (paragraph 25). Given the combined teachings of the references above show that phenols, salts, dodecyl benzene sulfonate and polyol, such as m-Cresol, alter the structure of a prion protein, there would have been a reasonable expectation of success in the inactivation of the prion protein (see Prusiner discussion above). The invention as a whole was clearly *prima facie* obvious to the ordinary artisan at the time the invention was made.

Conclusion

Of note, the claims are drawn to prions of all conformational states, including the native and the diseased state. Further, there is no novel gain of function in combining the elements discussed above in inactivating such proteins. Given all of the elements have been taught in the art as claimed, no claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner

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